Affiliated Genetics
2749 East Parleys Way, Suite 100
Salt Lake City, UT 84109
CLIA ID: 46D1077919

Affiliated Pharmarisk Psychiatric Created for:

Patient:
HIPAA Compliant Fax:
Physician:
Address:
Collection Date:
Specimen Type:

Accession #:
Gender:
DOB:
Received Date:
Report Generated:

Key Test Findings

Pharmacogenetic Results				
	Assay	Results	Phenotype	Clinical Consequences
✓	ANKK1/DRD2	DRD2:Taq1A GG	Unaltered DRD2 function	Consistent with a normal dopamine receptor D2 function.
⚠	COMT	Val158Met AG	Intermediate COMT Activity	Consistent with a reduced catechol O-methyltransferase (COMT) function.
✓	CYP1A2	*1F/*1F	Normal Metabolizer - Higher Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid Metabolism occurs in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
✓	CYP2B6	*1/*1	Normal Metabolizer	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
⚑	CYP2C19	*1/*17	Rapid Metabolizer	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
✓	CYP2C9	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
⚑	CYP2D6	*1/*1 XN	Rapid Metabolizer	Consistent with a significant increase in CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
✓	CYP3A4	*1/*1	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
✓	CYP3A5	*3/*3	Poor Metabolizer	Consistent with a poor CYP3A5 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
⚑	UGT2B15	*2/*2	Poor Metabolizer	Consistent with a decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.

Medication Guidance

Psychotropic Medications

Standard Precautions	Use With Caution	Consider Alternatives
Amphetamine (Adderall)	Clozapine (Clozaril)	Amitriptyline (Elavil)
Aripiprazole (Abilify)	Dexmethylphenidate (Focalin)	Atomoxetine (Strattera)
Bupropion (Wellbutrin)	Diazepam (Valium)	Citalopram (Celexa)
Clobazam (Onfi)	Donepezil (Aricept)	Clomipramine (Anafranil)
Desvenlafaxine (Pristiq)	Lorazepam	Desipramine (Norpramin)
Dextroamphetamine (Dexedrine)	Methylphenidate (Ritalin)	Doxepin (Silenor)
Duloxetine (Cymbalta)	Olanzapine (Zyprexa)	Escitalopram (Lexapro)
Galantamine (Razadyne)	Oxazepam	Haloperidol (Haldol)
Iloperidone (Fanapt)	Perphenazine (Trilafon)	Imipramine (Tofranil)
Lisdexamfetamine (Vyvanse)	Pimozide (Orap)	Nortriptyline (Pamelor)
Mirtazapine (Remeron)	Tetrabenazine (Xenazine)	Paroxetine (Paxil)
Naltrexone (Vivitrol)		Risperidone (Risperdal)
Paliperidone (Invega)		Trimipramine (Surmontil)
Phenytoin (Dilantin)		Venlafaxine (Effexor)
Sertraline (Zoloft)		
Thioridazine (Mellaril)		

Cardiovascular Medications

Standard Precautions	Use With Caution	Consider Alternatives
Atorvastatin (Lipitor)	Clopidogrel (Plavix)	Flecainide (Tambocor)
Carvedilol (Coreg)	Mexiletine (Mexitil)	Metoprolol (Lopressor)
Fluvastatin (Lescol)	Propafenone (Rythmol)	
Irbesartan (Avapro)		
Lovastatin (Mevacor)		
Nebivolol (Bystolic)		
Pitavastatin (Livalo)		
Prasugrel (Effient)		
Pravastatin (Pravachol)		
Propranolol (Inderal)		
Rosuvastatin (Crestor)		
Simvastatin (Zocor)		
Ticagrelor (Brilinta)		
Timolol (Timoptic)		
Warfarin (Coumadin)		

Pain Medications

Standard Precautions	Use With Caution	Consider Alternatives
Celecoxib (Celebrex)	Carisoprodol (Soma)	Codeine (Codeine)
Flurbiprofen (Ansaid)	Fentanyl (Actiq)	Tramadol (Ultram)
Methadone (Dolophine)	Hydrocodone (Vicodin)	
Morphine (MS Contin)	Tizanidine (Zanaflex)	
Oxycodone (Percocet)		
Piroxicam (Feldene)		

Other Medications

Standard Precautions	Use With Caution	Consider Alternatives
Darifenacin (Enablex)	Dexlansoprazole (Dexilant)	Ondansetron (Zofran)
Fesoterodine (Toviaz)	Esomeprazole (Nexium)	
Glimepiride (Amaryl)	Lansoprazole (Prevacid)	
Glipizide (Glucotrol)	Omeprazole (Prilosec)	
Glyburide (Micronase)	Pantoprazole (Protonix)	
Rabeprazole (Aciphex)	Voriconazole (Vfend)	
Tacrolimus (Prograf)		
Tamsulosin (Flomax)		
Tolbutamide (Orinase)		
Tolterodine (Detrol)		

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Test Details

Gene	Alleles Tested
ANKK1/DRD2	DRD2:Taq1A
COMT	Val158Met
CYP1A2	*1C, *1D, *1F, *1K, *1L, *1V
CYP2B6	*4, *5, *11, *9, *6, *8, *18, *22, *28
CYP2C19	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *12, *17
CYP2C9	*2, *3, *4, *5, *6, *8, *10, *11, *25
CYP2D6	*2, *11, *15, *3, *4, *4M, *6, *7, *8, *10, *12, *14A, *17, *18, *19, *20, *38, *29, *35, *44, *41, *56, *5 (gene deletion), XN (gene duplication)
CYP3A4	*22, *1B, *2, *3, *12, *17
CYP3A5	*1D, *2, *3, *3C, *5, *6, *7, *8, *9
UGT2B15	*2

Methodology:

Testing is performed on DNA extracted from a buccal swab. Samples are genotyped using Taqman® allele discrimination assays. The assays detect alleles listed above, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Limitations:

The interpretations provided in this report are provided to assist health care providers, but they are not a treatment recommendation. Diagnosis and treatment remain the sole responsibility of the ordering physician. While the polymorphisms tested are important, other variants and mutations in these genes will not be detected. Mutations in other genes that could affect drug metabolism will not be detected. Non-genetic factors also affect metabolism. This test is not a substitute for clinical and therapeutic drug monitoring. This report does not address patient drug allergies or drug-drug interactions.

Signature:

Kenneth Ward M.D.

Date: 1/29/2014

CLIA FDA Statement:

This Laboratory Developed Test was developed and its performance characteristics determined by Affiliated Genetic, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing and has established and verified the test's accuracy. This test has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. These results are adjunctive to an ordering physician's diagnosis.

Appendix: Dosing Guidance

Amitriptyline (Elavil)

Increased Sensitivity to Amitriptyline (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing amitriptyline at standard dose and monitor the plasma concentrations of amitriptyline and nortriptyline to guide dose adjustments.

Atomoxetine (Strattera)

Non-Response to Atomoxetine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider prescribing atomoxetine with careful titration and monitoring for reduced efficacy. There is insufficient data to calculate dose adjustment. Or consider alternative drug such as methylphenidate.

Carisoprodol (Soma)

Altered Sensitivity to Carisoprodol (CYP2C19 *1/*17 Rapid Metabolizer)

There is insufficient data to allow calculation of dose adjustment and if carisodoprol is prescribed, it is recommended to use a lower dose and to carefully monitor the patient for side effects.

Citalopram (Celexa)

Insufficient Response to Citalopram (CYP2C19 *1/*17 Rapid Metabolizer)

The patient may not respond to usual doses. Monitor plasma concentration and increase dose to a maximum of 150% in response to efficacy and adverse events or select alternative drug.

Clomipramine (Anafranil)

Increased Sensitivity to Clomipramine (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing clomipramine at standard dose and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to guide dose adjustments.

Clopidogrel (Plavix)

Increased Response to Clopidogrel (CYP2C19 *1/*17 Rapid Metabolizer)

Clopidogrel can be prescribed at standard label-recommended dosage. Individuals with the *17 allele may have an increased risk of bleeding while taking clopidogrel.

Clozapine (Clozaril)

Non-Response to Clozapine (CYP1A2 *1F/*1F Normal Metabolizer - Higher Inducibility)

Smokers have a high risk for non-response and may require higher doses. There is an association between high clozapine doses and the risk of seizures, therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels leading to adverse events and therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Codeine (Codeine)

Increased Response to Codeine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Avoid prescribing codeine and consider alternative opioids other than tramadol or consider a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids (not sensitive to CYP2D6 function) include: Fentanyl, Morphine, Hydromorphone, Oxymorphone, Tapentadol and Meperidine.

Desipramine (Norpramin)

Non-Response to Desipramine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider alternative drug or prescribe desipramine at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to desipramine and metabolites plasma concentrations and clinical response.

Dexlansoprazole (Dexilant)

Possible Insufficient Response to Dexlansoprazole (CYP2C19 *1/*17 Rapid Metabolizer)

Be alert to insufficient response and **consider dose increase**. There is insufficient data to allow calculation of dose adjustment.

Dexmethylphenidate (Focalin)

Decreased Response to Dexmethylphenidate (COMT Val158Met AG Heterozygous Val158Met)

The patient's genotype predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and responses of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Diazepam (Valium)

Altered Sensitivity to Diazepam (CYP2C19 *1/*17 Rapid Metabolizer)

There is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the response and adjust the dose accordingly or select an alternative drug.

Donepezil (Aricept)

Possible Altered Response to Donepezil (CYP2D6 *1/*1 XN Rapid Metabolizer)

When compared to a normal metabolizer, a rapid metabolizers has a 24% increase in donepezil clearance; the clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Doxepin (Silenor)

Increased Sensitivity to Doxepin (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing doxepin at standard dose and monitor the plasma concentrations of doxepin and desmethyl-doxepin to guide dose adjustments.

Escitalopram (Lexapro)

Insufficient Reponse to Escitalopram (CYP2C19 *1/*17 Rapid Metabolizer)

Monitor plasma concentration and titrate dose to a maximum of 150% in response to efficacy and adverse events or select alternative drug.

Esomeprazole (Nexium)

Insufficient Response to Esomeprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 50-100% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 50-100%.

Flecainide (Tambocor)

Altered Response to Flecainide (CYP2D6 *1/*1 XN Rapid Metabolizer)

Titrate carefully and consider adjusting dose in response to plasma concentration and ECG monitoring OR consider alternative drug. Example of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine and amiodarone.

Haloperidol (Haldol)

Non-Response to Haloperidol (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider alternative drug or prescribe haloperidol at standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations. Available alternative drugs include: pimozide; fluphenazine, quetiapine, olanzapine and clozapine.

Imipramine (Tofranil)

Increased Sensitivity to Imipramine (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing imipramine at standard dose and monitor the plasma concentrations of imipramine and desipramine to guide dose adjustments.

Lansoprazole (Prevacid)

Insufficient Response to Lansoprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 200%.

Lorazepam (Ativan)

Possible Altered Response to Lorazepam (UGT2B15 *2/*2 Poor Metabolizer)

Lorazepam clearance is reduced in this patient. However, there is insufficient evidence as to whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Methylphenidate (Ritalin)

Decreased Response to Methylphenidate (COMT Val158Met AG Heterozygous Val158Met)

The patient's genotype predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and responses of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Metoprolol (Lopressor)

Possible Non-Responder to Metoprolol (CYP2D6 *1/*1 XN Rapid Metabolizer)

Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol or or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Mexiletine (Mexitil)

Altered Response to Mexiletine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring until a favorable response in achieved.

Nortriptyline (Pamelor)

Non-Response to Nortriptyline (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider alternative drug or prescribe nortriptyline at increased dose and monitor the plasma concentration of amitryptyline and hydroxynortriptyline. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Olanzapine (Zyprexa)

Non-Response to Olanzapine (CYP1A2 *1F/*1F Normal Metabolizer - Higher Inducibility)

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels leading to adverse events and therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Omeprazole (Prilosec)

Insufficient Response to Omeprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 100-200%.

Ondansetron (Zofran)

Non-Response to Ondansetron (CYP2D6 *1/*1 XN Rapid Metabolizer)

A substantially decreased antiemetic effect has been reported in CYP2D6 rapid metabolizers. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Oxazepam (Serax)

Possible Altered Response to Oxazepam (UGT2B15 *2/*2 Poor Metabolizer)

Oxazepam clearance is reduced in this patient. However, there is insufficient evidence as to whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Pantoprazole (Protonix)

Insufficient Response to Pantoprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 400% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 400%.

Paroxetine (Paxil)

Non-Response to Paroxetine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider alternative drug or increase paroxetine dose and adjust dosage in response to efficacy. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Perphenazine (Trilafon)

Possible Non-Response to Perphenazine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Subjects with increased CYP2D6 function will metabolize perphenazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Pimozide (Orap)

Possible Non-Response to Pimozide (CYP2D6 *1/*1 XN Rapid Metabolizer)

There is insufficient data to calculate dose adjustment and if pimozide is prescribed at standard dosing, monitor response and be alert to reduced efficacy. Standard starting dose: 1 to 2 mg/day (adult) or 0.05 mg/kg/day (children) - Doses may be increased to a maximum of 10 mg/day or 0.2 mg/kg/day.

Propafenone (Rythmol)

Altered Response to Propafenone (CYP2D6 *1/*1 XN Rapid Metabolizer)

There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust dose in response to plasma concentration and ECG monitoring. OR consider alternative drug such as sotalol, disopyramide, quinidine and amiodarone.

Risperidone (Risperdal)

Non-Response to Risperidone (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider alternative drug; available alternative drugs include: quetiapine, olanzapine, clozapine. Or prescribe risperidone and be extra alert to insufficient response and adjust dosage in response to clinical response and adverse events.

Tetrabenazine (Xenazine)

Unknown Sensitivity to Tetrabenazine (CYP2D6 *1/*1 XN Rapid Metabolizer)

There is insufficient data to calculate dose adjustment and if tetrabenazine is prescribed, individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 rapid metabolizers is not defined. The maximum daily dose in normal metabolizers is 100 mg with a maximum single dose of 37.5 mg.** If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Tizanidine (Zanaflex)

Possible Non-Response to Tizanidine (CYP1A2 *1F/*1F Normal Metabolizer - Higher Inducibility)

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation, therefore careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Tramadol (Ultram)

Increased Response to Tramadol (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider reducing tramadol dose by 30%. Careful monitoring for side effects and weekly titration are recommended. If toxicity, consider alternative opioids other than codeine or consider a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids (not sensitive to CYP2D6 function) include: Fentanyl, Morphine, Hydromorphone, Oxymorphone, Tapentadol and Meperidine.

Trimipramine (Surmontil)

Increased Sensitivity to Trimipramine (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing trimipramine at standard dose and monitor the plasma concentrations of trimipramine and desmethy-ltrimipramine to guide dose adjustments.

Venlafaxine (Effexor)

Non-Response to Venlafaxine (CYP2D6 *1/*1 XN Rapid Metabolizer)

Consider alternative drug; available alternative drugs include: citalopram and sertraline. Or, increase venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Voriconazole (Vfend)

Non-response to Voriconazole (CYP2C19 *1/*17 Rapid Metabolizer)

Voriconazole plasma concentrations may be low when standard dosage is used, increasing the risk of loss of response and effectiveness. Closely monitor voriconazole plasma concentrations and adjust the dose accordingly.

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Prescription Alert

DOB

This individual has been tested for gene variants that may affect medications prescribed.

GENE	RESULT
ANKK1	Unaltered DRD2 function
COMT	Intermediate COMT Activity
CYP1A2	Normal Metabolizer - Higher Inducibility
CYP2B6	Normal Metabolizer
CYP2C19	Rapid Metabolizer
CYP2C9	Normal Metabolizer
CYP2D6	Rapid Metabolizer
CYP3A4	Normal Metabolizer
CYP3A5	Poor Metabolizer
UGT2B15	Poor Metabolizer

Healthcare Providers: For up-to-date information concerning the impact of these genetic tests on drug precribing by may consult the PharmGKB database:

www.pharmgkb.org

Note:This patient has also been tested for common variants in the Factor II, Factor V, MTHFR, and ApoE genes.These results are available on the patient's medical records.